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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,006	02/01/2001	Thomas Hottkowitz	2923-123	6539

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EXAMINER

STOCKTON, LAURA LYNNE

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/762,006

Applicant(s)

HOTTKOWITZ, THOMAS

Examiner

Laura L. Stockton, Ph.D.

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 4, 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13, 15, 33 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13, 15, 33 and 43-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1626

DETAILED ACTION

Claims 1-13, 15, 33 and 43-45 are pending in the application.

Election/Restrictions

Applicants' election with traverse of Group XI, and the species of compound 372 in Paper No. 9 (filed June 14, 2002), was acknowledged in the Office Action mailed July 11, 2002 {Paper No. 10}. The requirement has deemed proper and made FINAL in a previous Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1626

Claims 1-13, 15, 33 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support in the specification or the originally filed claims for the expression " $15 \leq p+q \leq 30$ " found in claims 1, 44 and 45. Applicants did not state where in the specification {page numbers(s) and line number(s)} support could be found for the amendment to the claims. Applicants should specifically point out the support for any amendments. See M.P.E.P. §§ 714.02 and 2163.06. Therefore, the claims lack written description as such.

Art Unit: 1626

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13, 15, 33 and 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 lacks antecedent basis from claim 1 for the same reason given in the previous Office Action.

Response to Arguments

Applicants' arguments filed May 4, 2006 have been fully considered. Applicants state that the rejection of claim 15 has been overcome by amending claims 1, 44 and 45. In response, since claim 15 was not also amended, the claim is properly rejected for lacking antecedent basis.

Art Unit: 1626

Response to Amendment

The Declaration by Dr. H. Eibl filed December 15, 2004 is insufficient to overcome the rejection of claims 1-13, 15, 33 and 43-45 based upon 35 U.S.C. 103(a) as being unpatentable over AT 393505 and Eibl et al. {EP 534,445} as set forth in the last Office action because the Declaration is not executed. Further, the closest prior art compound(s) is not identified. Applicant relying upon comparative showing to rebut *prima facie* case must compare his claimed invention with the closest prior art. In re Holladay, 199 USPQ 516, 1978.

Additionally, Applicants did not identify which of their specifically disclosed specie, presently under examination, is being compared to the prior art {e.g., instant Compound 372 found on page 60 of the instant specification}. Also, ALPC appears to stand for a number of compounds {see 4)} in the Table on page 4 at

Art Unit: 1626

the bottom} but separate data is not given for each compound other than its molecular weight.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13, 15, 33 and 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over AT 393505 and Eibl et al. {EP 534,445}, each taken alone. English translations of AT 393505 and Eibl et al. have been provided with a previous Office Action and will be referred to hereinafter unless otherwise specified.

Determination of the scope and content of the prior art (MPEP

§2141.01)

Art Unit: 1626

Applicants claim phosphates and phosphoamines. AT 393505 teaches phosphates and phosphoamines which are structurally similar to the instant claimed compounds {see pages 3, 4, 17 and 21-25; and especially Example 13 (page 41) and Example 14 (pages 42-43)}. Eibl et al. also teach phosphate esters which are structurally similar to the instant claimed compounds {page 2, lines 25-42 and Example 5 (Beispiel 5) on page 6 in the EP document; and pages 3-8 in the English translation}.

Ascertainment of the difference between the prior art and the claims

(MPEP §2141.02)

The difference between the compounds of the prior art and the compounds instantly claimed is that the instant claimed compounds are generically described in the prior art.

Art Unit: 1626

***Finding of prima facie obviousness--rational and motivation (MPEP
§2142-2413)***

The indiscriminate selection of "some" among "many" is *prima facie* obvious. The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., cytotoxic activity).

One skilled in the art would thus be motivated to prepare compounds embraced by the prior art to arrive at the instant claimed compounds with the expectation of obtaining additional beneficial products which would have cytotoxic activity and can be used to treat tumors. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Response to Arguments

Applicants' arguments filed May 4, 2006 have been fully considered. Applicants argue that the claims

Art Unit: 1626

recite that "A is a radical having at least 19 carbon atoms and thus the double bond in variable A is at a distance from the O (oxygen linkage in variable A) which does not appear in a naturally-occurring corresponding radical and that such structural variations in the apolar region lead to compounds lead to compounds exhibiting improved anti-tumor activity.

Applicants argue that the instant claimed compounds exhibit further surprising advantages over the cited prior art compounds in that although the prior art compounds show good anti-tumor activity, the prior art compounds exhibit significant toxicity, such as hemolysis and thrombophlebitis and therefore such compounds having a short carbon chain cannot be administered intravenously but rather only orally where toxicity is not a problem. Applicants further argue that, in contrast, it has been surprisingly found that the toxicity problems known in the art no longer occur with compounds having a double bond in a non-naturally

Art Unit: 1626

occurring position, as claimed in the present invention and that the tumor-effective concentrations of these compounds are no longer toxic. Applicants argue that this is demonstrated in the tests concerning (Z)-10-docosenyl-1-phosphocholine submitted with Applicants' December 15, 2004 response. Applicants argue that it is impractical to present the side-by-side comparison that the Examiner is seeking given what is a difficult and complicated procedure to prepare hexadecenylphosphocholine.

All of Applicants' arguments have been considered but have not been found persuasive. Applicants claim phosphates and phosphoamines. AT 393505 teaches phosphates and phosphoamines, which are structurally similar to the instant claimed compounds, that can be administered topically, orally or intravenously {see above noted pages}. Eibl et al. also teach phosphate esters, which are structurally similar to the instant claimed compounds, that can be administered topically

Art Unit: 1626

or orally {see above noted pages}. Applicants have not provided the Office with factual persuasive evidence that is demonstrated in a persuasive side-by-side showing of unexpected, beneficial, and superior results of the instant claimed compounds, under examination, over the specie prepared in the cited prior art.

Attorney's arguments of unexpected results cannot take the place of evidence in the record. In re DeBlauwe, 222 U.S.P.Q. 191, 196 (Fed. Cir. 1984). As stated above, Applicant relying upon comparative showing to rebut a *prima facie* case must compare his claimed invention with the closest prior art. In re Holladay, 199 USPQ 516, 1978. Further, the ineffectiveness of the unexecuted Declaration by Dr. H. Eibl filed December 15, 2004 has been discussed above.

Applicants' argument concerning the allege impracticality to present the side-by-side comparison that the Examiner is seeking given what is a difficult and complicated procedure to prepare

Art Unit: 1626

hexadecenylphosphocholine has been considered. This argument is not persuasively since the claims, as originally filed, embraced a compound in AT 393505 so much so that a compound in the AT 393505 reference anticipated the claims {see the Office Action dated July 11, 2002}. Further, Applicants' specification discloses a vast number of tables each having a multitude of specie, including "hexadecenyl-1-phosphochloine" as found on page 39 of the instant specification. Are Applicants stating, or suggesting, on the record that the instant claimed invention lacks enablement under 35 USC 112, first paragraph on how to make? Therefore, Applicants' argument is not persuasive. The rejection of the claims is deemed proper and is therefore maintained.

Conclusion

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action.

Art Unit: 1626

Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

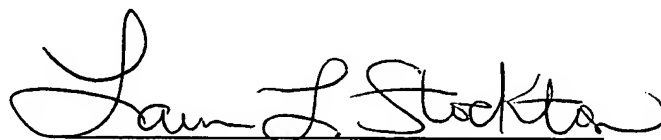
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached

Art Unit: 1626

on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

A handwritten signature in cursive script, reading "Laura L. Stockton".

Laura L. Stockton, Ph.D.
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

July 24, 2006